



Armed Forces College of Medicine AFCM



Respiratory chain (ETC) and shuttle mechanisms

By

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INTENDED LEARNING OBJECTIVES (ILO)



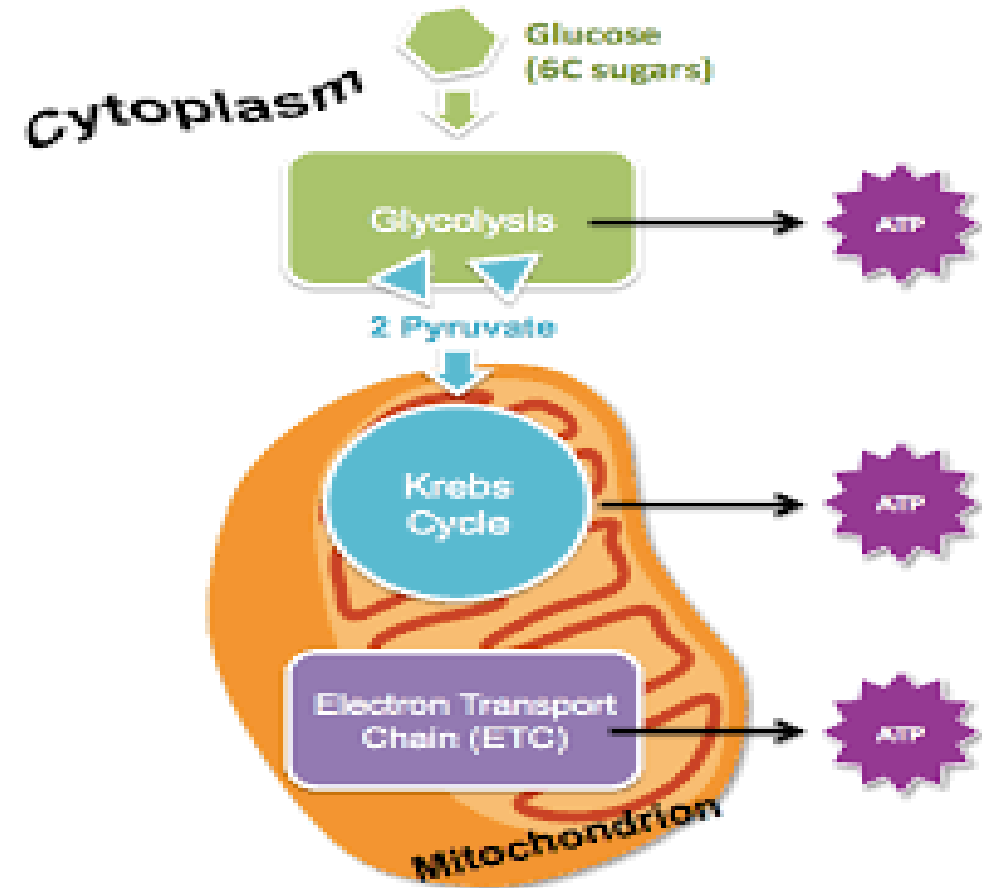
• *By the end of this lecture the student will be able to:*

1. Explain the relationship between the cellular respiration and Energy production.
2. Identify the importance of mitochondria in the cellular respiration.
3. Discuss the shuttle mechanisms used to transport the reducing equivalents from the cytoplasm into the mitochondria.
4. Mention the sources of ATP.
5. Discuss the components of the ETC & their arrangement on the inner mitochondrial membrane.

Cellular respiration

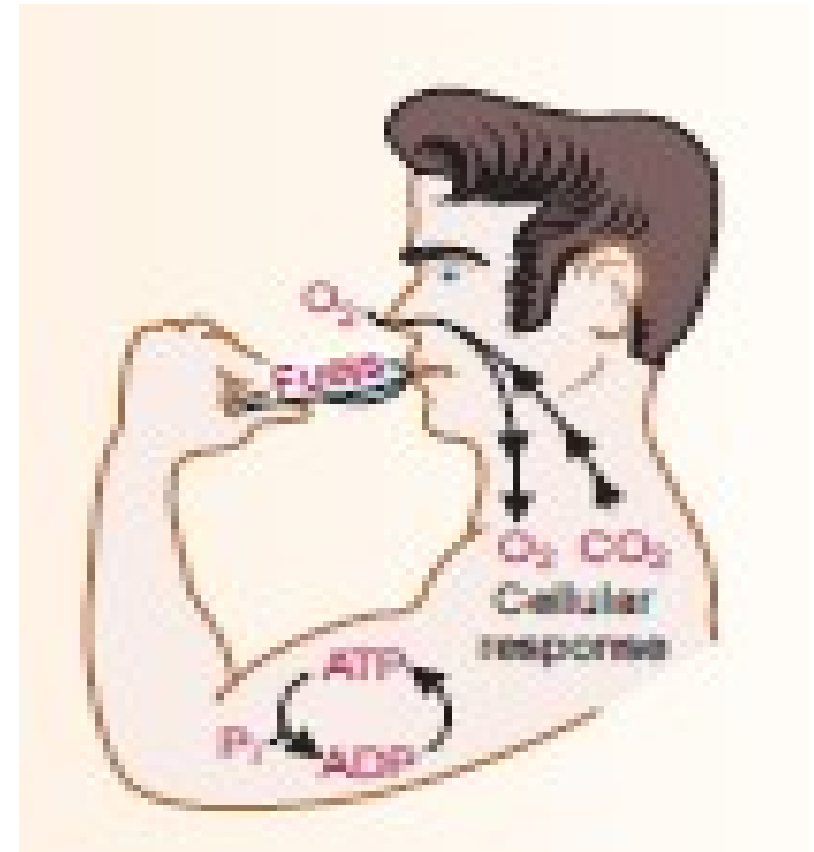


- The overall process of using **O₂** and **energy** derived from oxidizing fuels to generate **ATP**.



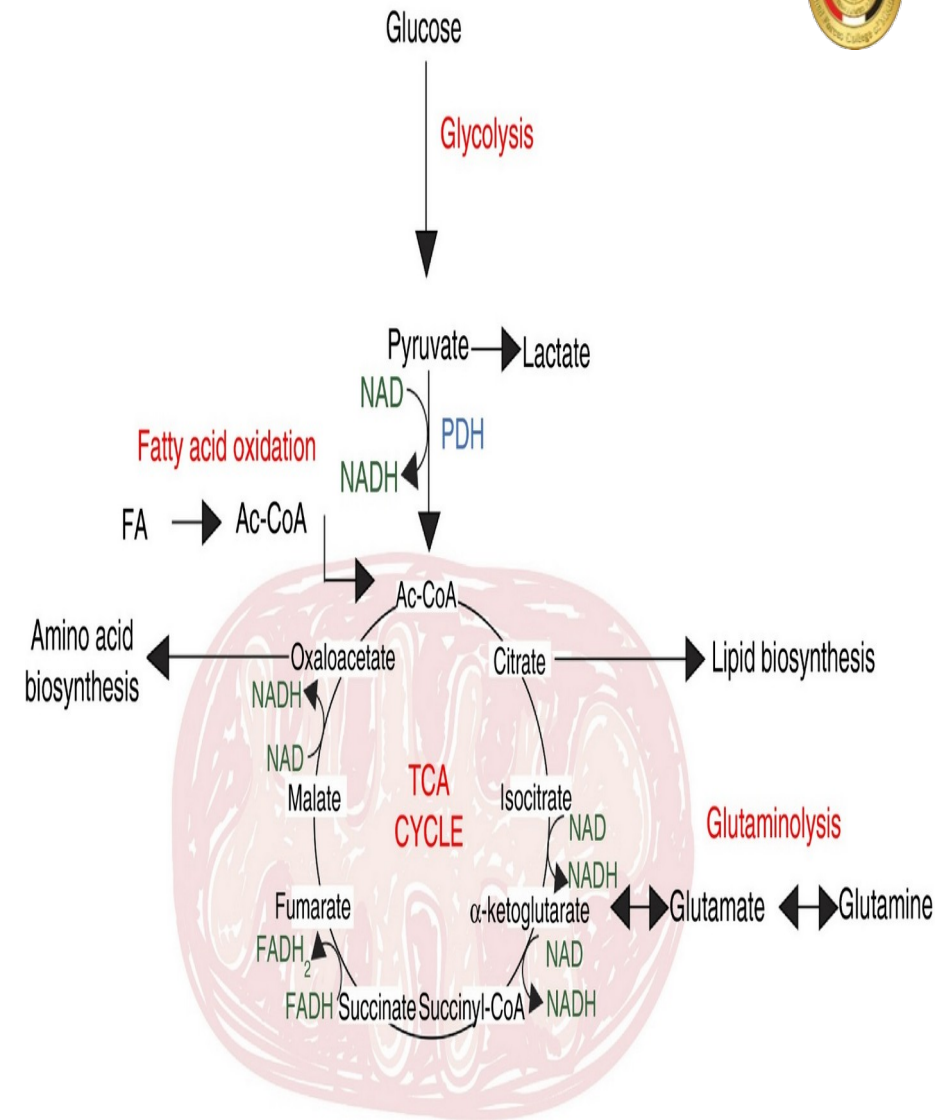


- **We need to breathe principally because our cells require O_2 to generate adequate amounts of ATP from the oxidation of fuels to CO_2 .**



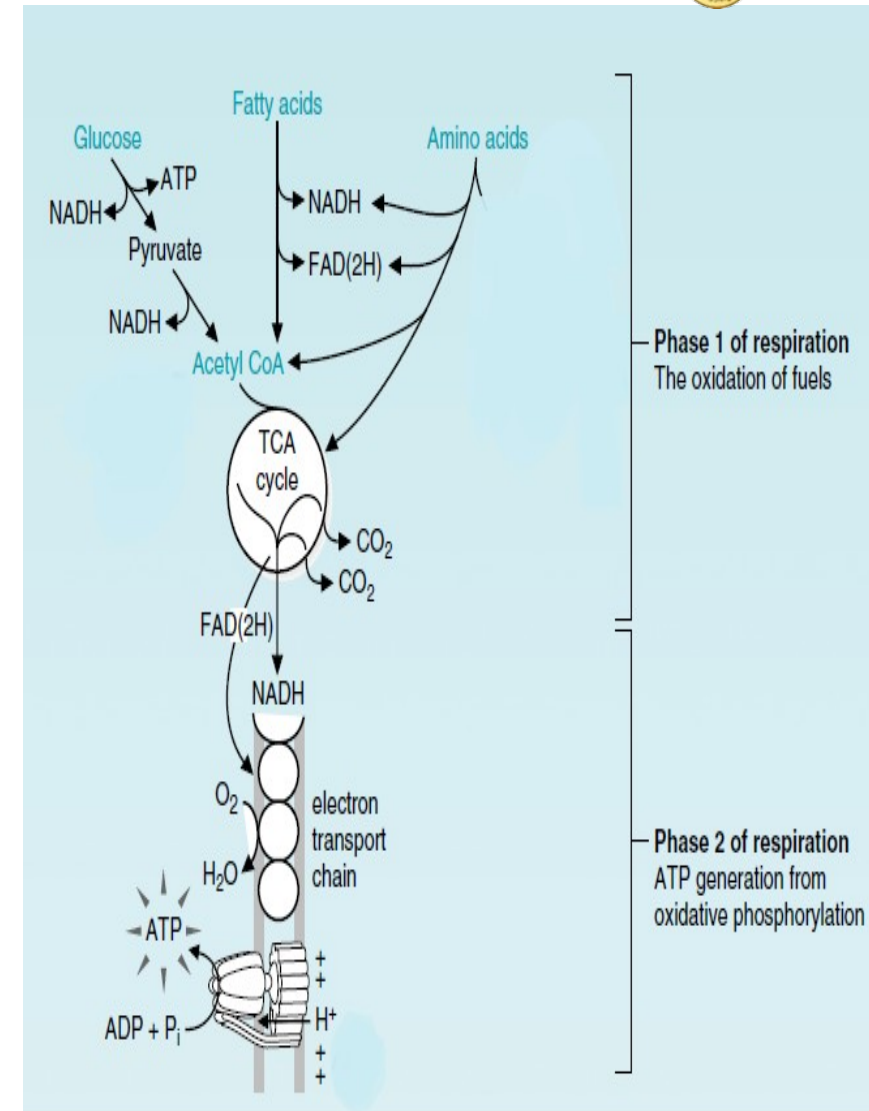


- The pathways for the **oxidation of most fuels** (glucose, fatty acids, and many amino acids) converge on the generation of **acetyl CoA**.
- - The **complete oxidation** of the **acetyl group** to **CO₂** occurs in the **tricarboxylic acid (TCA) cycle**, which collects the energy mostly as **NADH** and **FADH₂**.





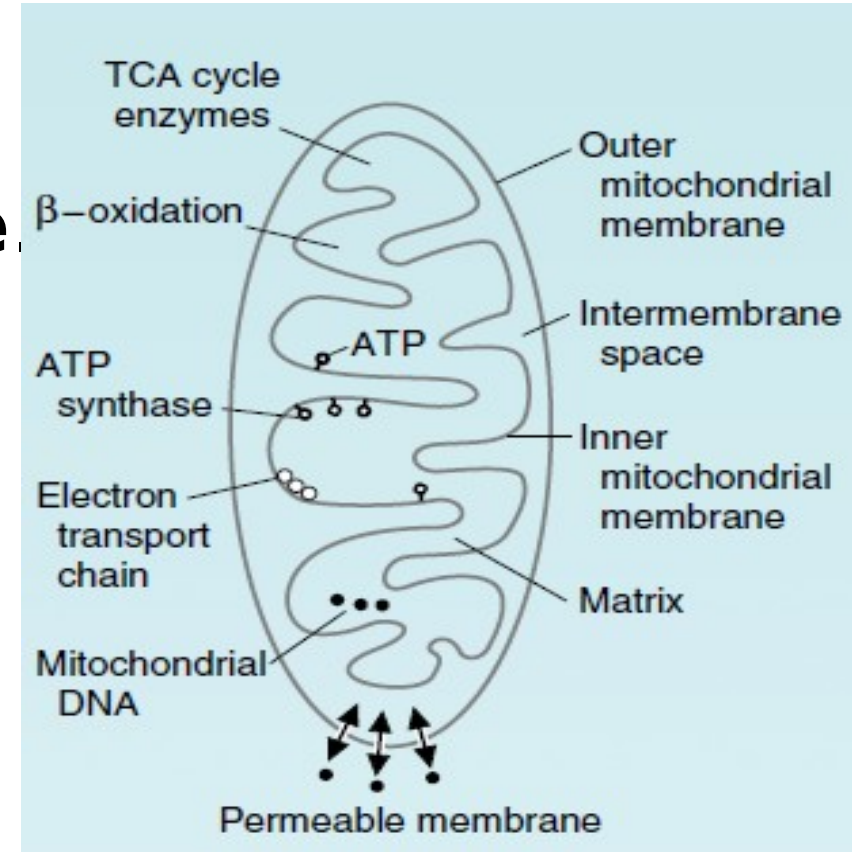
- The **energy derived from fuel oxidation** is converted to the high-energy phosphate bonds of **ATP** by the process of **oxidative phosphorylation**.
- - Electrons are transferred from NADH and FADH₂ to O₂ by the **electron transport chain (ETC)**, located in the inner mitochondrial membrane). These series of reactions are coupled with the **synthesis of ATP**.



Site of cellular respiration; ***Mitochondria***



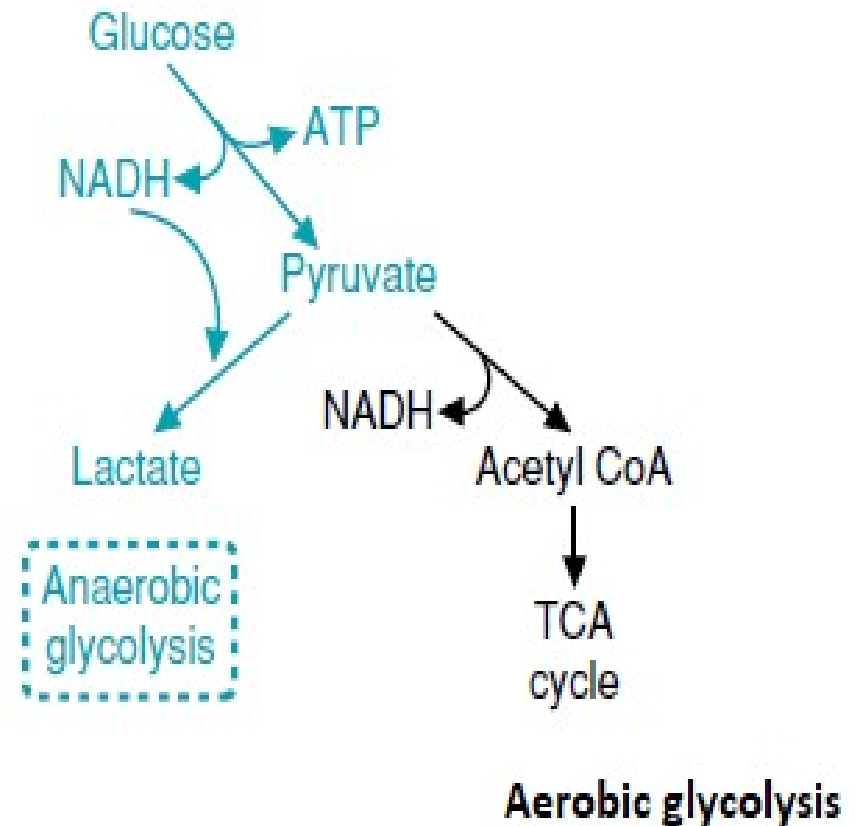
- The components of the ETC are located in the **inner mitochondrial membrane**.
- - The **mitochondrial matrix** (the compartment enclosed by the inner mitochondrial membrane) contains, however, almost all of the **enzymes for the TCA cycle** and **oxidation of fatty acids**).



Glycolysis as an example of cellular respiration

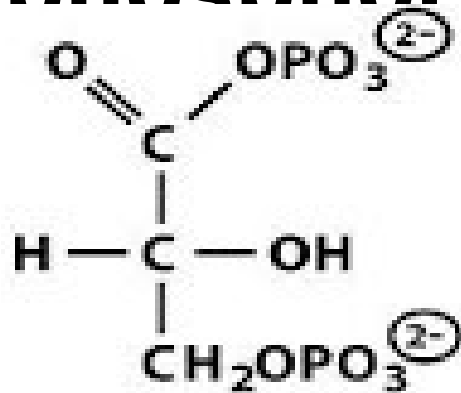


- **Glucose** is a universal fuel used to generate ATP in every cell type in the body.
- In glycolysis, **1** mole of **glucose** is oxidized to **2** moles of **pyruvate** and **2** moles of **NADH** by cytosolic enzymes.

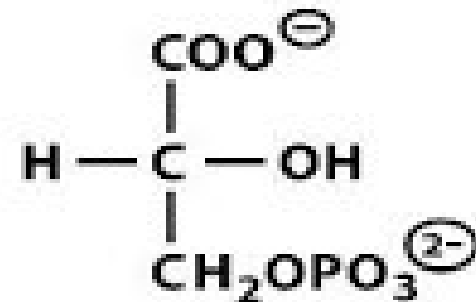
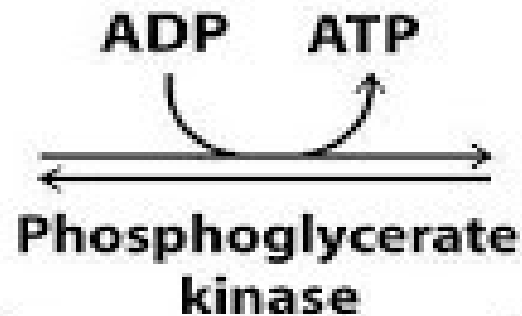




- Small amounts of **ATP** are generated when high-energy metabolic intermediates transfer phosphate to ADP in a process termed **substrate-level phosphorylation**



1,3-Bisphosphoglycerate



3-Phosphoglycerate

Fate of the $\text{NADH} + \text{H}^+$ during Aerobic glycolysis:

- NADH produced in the cytosol cannot pass through the inner mitochondrial membrane, to reach the respiratory chain and be oxidized.

It is indirectly transferred to inside the mitochondria by what is called the :shuttle mechanisms

- ***Glycerol-3P dehydrogenase shuttle***

- ***Malate-Aspartate shuttle***

Many tissues contain both the glycerophosphate shuttle and the malate-aspartate shuttle

Malate Aspartate shuttle

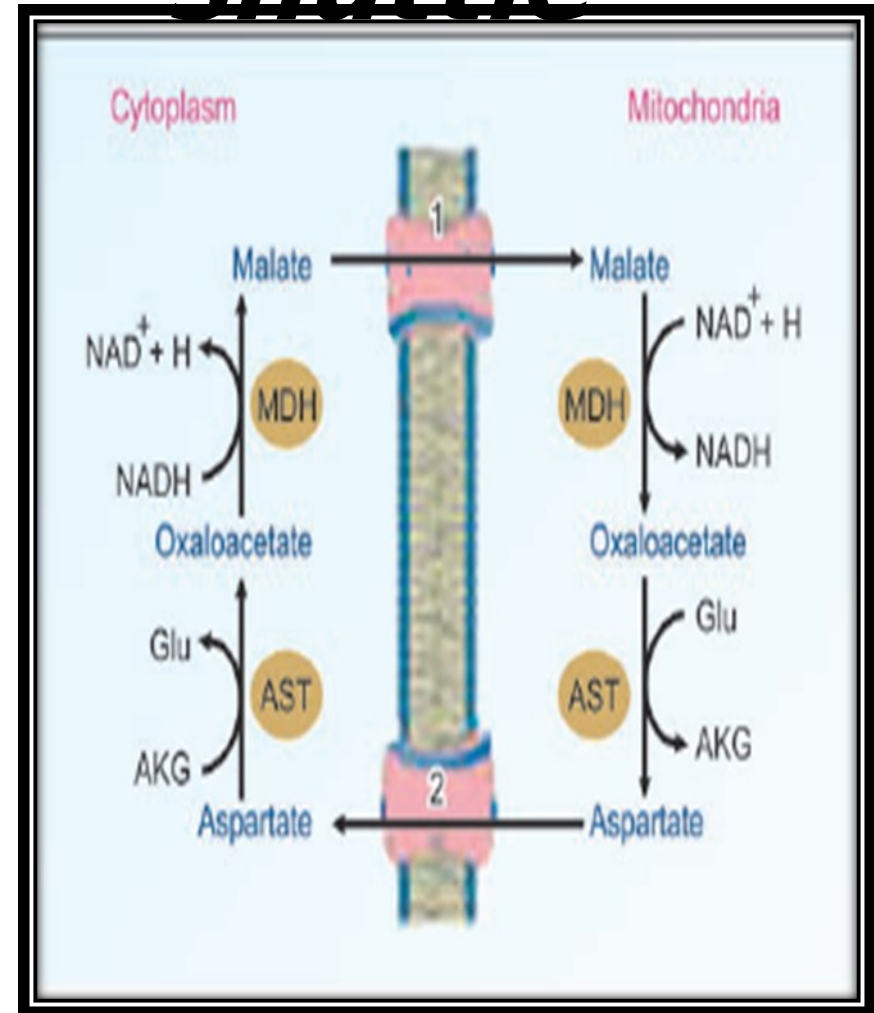
*The **cytosolic malate dehydrogenase** transfers electrons from **NADH** to **cytosolic oxaloacetate** to form **malate**.

*Malate is transported across the inner mitochondrial membrane by a specific translocase.

In the mitochondrial matrix, **malate** is oxidized **back to oxaloacetate** by **mitochondrial malate dehydrogenase**, and NADH is generated. This NADH can donate electrons to the electron transport chain with generation of approximately 3 moles of ATP per mole of NADH.

*The newly formed oxaloacetate cannot pass back through the inner mitochondrial membrane.

Therefore, oxaloacetate is converted by AST into aspartate. Aspartate is



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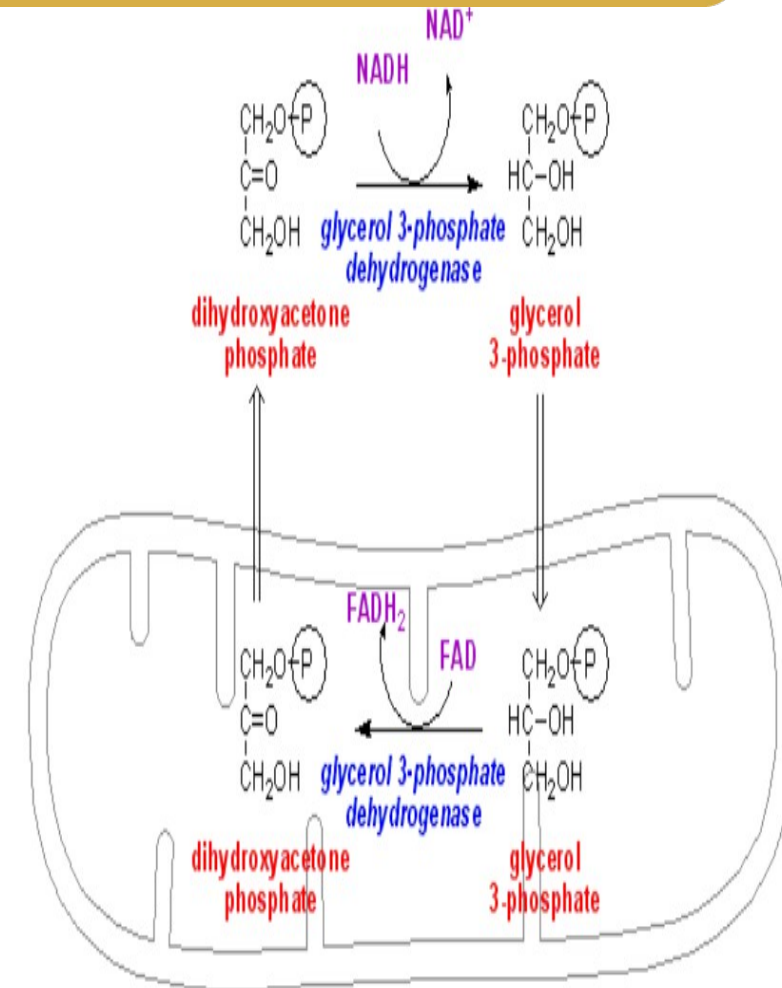


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The Glycerol 3- Phosphate Shuttle



- The glycerolphosphate shuttle is **the major shuttle** in most tissues.
- * In this shuttle, **cytoplasmic glycerol 3-phosphate dehydrogenase** transfers electrons from **NADH** to **DHAP** to form **glycerol 3-phosphate**
- * **Glycerol 3-phosphate** then **diffuses to the inner**



Student's activity



- ***So Malate-aspartate shuttle is more complex pathway but it is more economic than the glycerol phosphate shuttle. Why?***

CASE SCENARIO



- You are part of the team that is called to respond to a possible terrorist attack in an art museum.
- As fumes developed, several people started **choking and collapsing**. The museum authorities tell you 120 people are already pronounced **dead** at the scene.

Cyanide Poisoning



What Does ATP Do for You?



It supplies YOU with ENERGY!

It is the **energy currency** of the cell.





Formation Of ATP

The ATP/ADP cycle



Since the concentration of **ATP is very small** and meets the needs of the body
for few seconds

ATP is continuously
consumed and regenerated rapidly

Importance of ATP as a Source of Energy



- (1) Synthesis of Macromolecules:
DNA, RNA and proteins.
Glycogen and triacylglycerol.
Structural molecules: membranes.
- (2) Support the endergonic reactions in metabolic pathways.
- (3) Important for active transport across membranes.
- (4) Important for muscle contraction.

Formation of ATP



1- Substrate Level Phosphorylation

2- Oxidative Phosphorylation (Factory)

1. Substrate Level Phosphorylation



- Transfer of high group potential to incorporate P_i with high energy into ADP to form ATP.
- It may occur in cytosol or mitochondria.

The group transfer potential may be:

- -phosphates as 1,3 BPG, phosphoenolpyruvate “glycolysis” and creatineP “muscles”.
- -Succinyl CoA, a thioester can participate in substrate level phosphorylation “TCA cycle”.

2. Oxidative Phosphorylation *(Factory)*



Oxidative phosphorylation, the major energy – generating process of most cells occurs in the mitochondria. The mitochondria is called the power house of the cell.

By

Electron Transport Chain
(Respiratory Chain)

• ***Oxidation-Reduction***



■ **Oxidation**

Addition of oxygen

or removal of **hydrogen** or an electron

■ **Reduction**

Addition of an electron or hydrogen
or removal of oxygen

Student activity

What is meant by Reduction?

- a) Addition of oxygen
- b) Removal of hydrogen
- c) Removal of an electron
- d) Addition of hydrogen

Electron Transport Chain (Respiratory Chain)



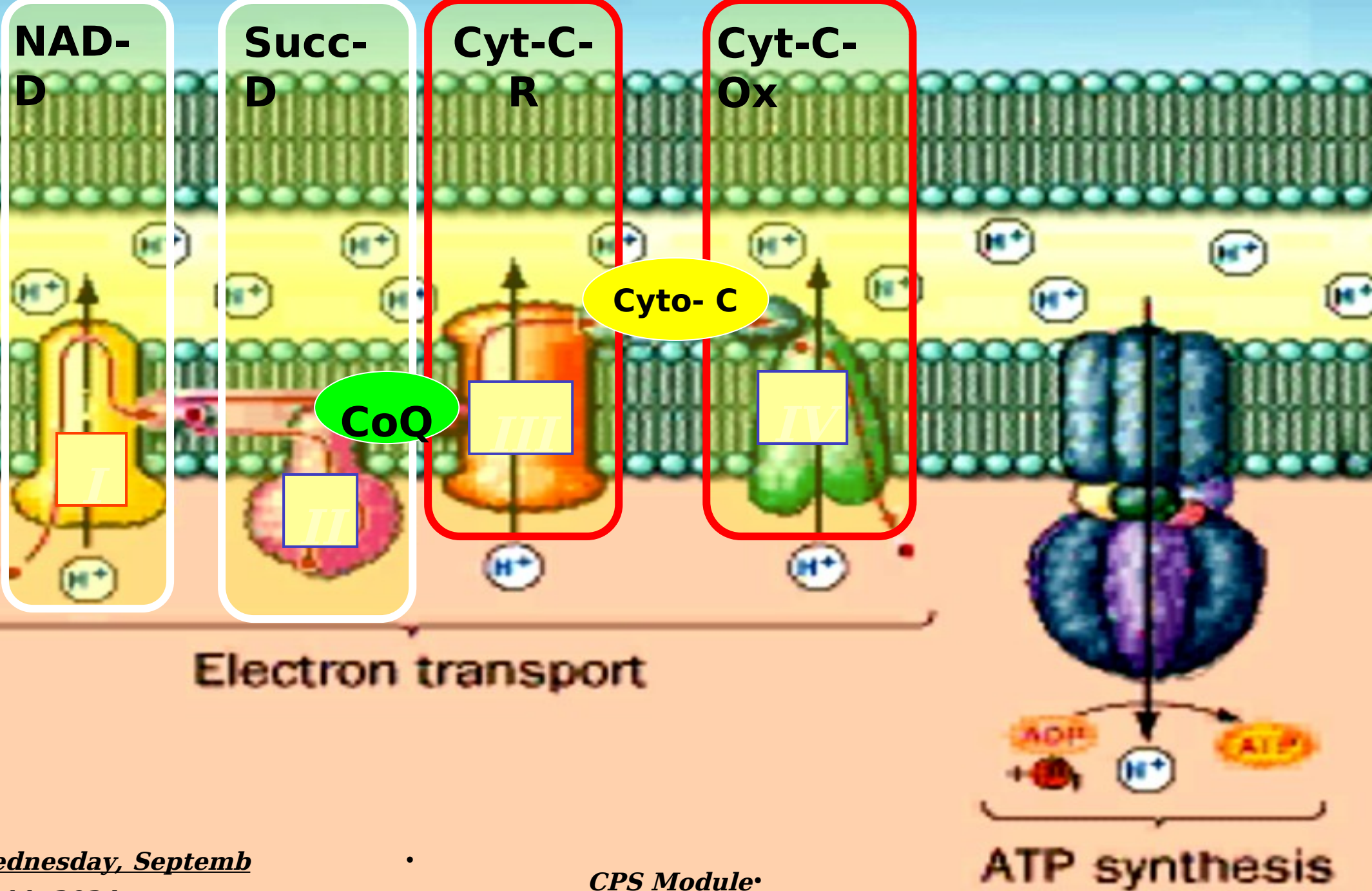
Definition



It is **a sequence of** enzymes & carriers which are located on the **inner mitochondrial membrane**.

It is responsible for the transport of electrons from reducing equivalents (**NADH** and **FADH₂**) to **O₂** to produce **H₂O**.

Also **It has the machinery** for **trapping** the liberated free energy to form ATP.



Three types of electron carriers function in the respiratory chain



- (1) Ubiquinone “Coenzyme Q”**
- (2) Cytochromes**
- (3) Iron - sulfur proteins:**

Ubiquinone “Coenzyme Q”



It is fat soluble benzoquinone (similar to vit K)

it is **freely diffusible within the lipid bilayer**

of the inner mitochondrial membrane

Acts as an intermediate electron carrier

Transfers electrons from Complex I, II

→ to complex III

Cytochrome C



Cytochromes are a class of proteins that contain a heme group tightly bound to the protein.

Three types (a, b and c) participate in the respiratory chain.

All are integral membrane proteins with exception of **cyt c**, a soluble free protein

Cytochrome c is an Intermediate electron carrier **Between** Complex **III** & **IV**

Iron - sulfur proteins



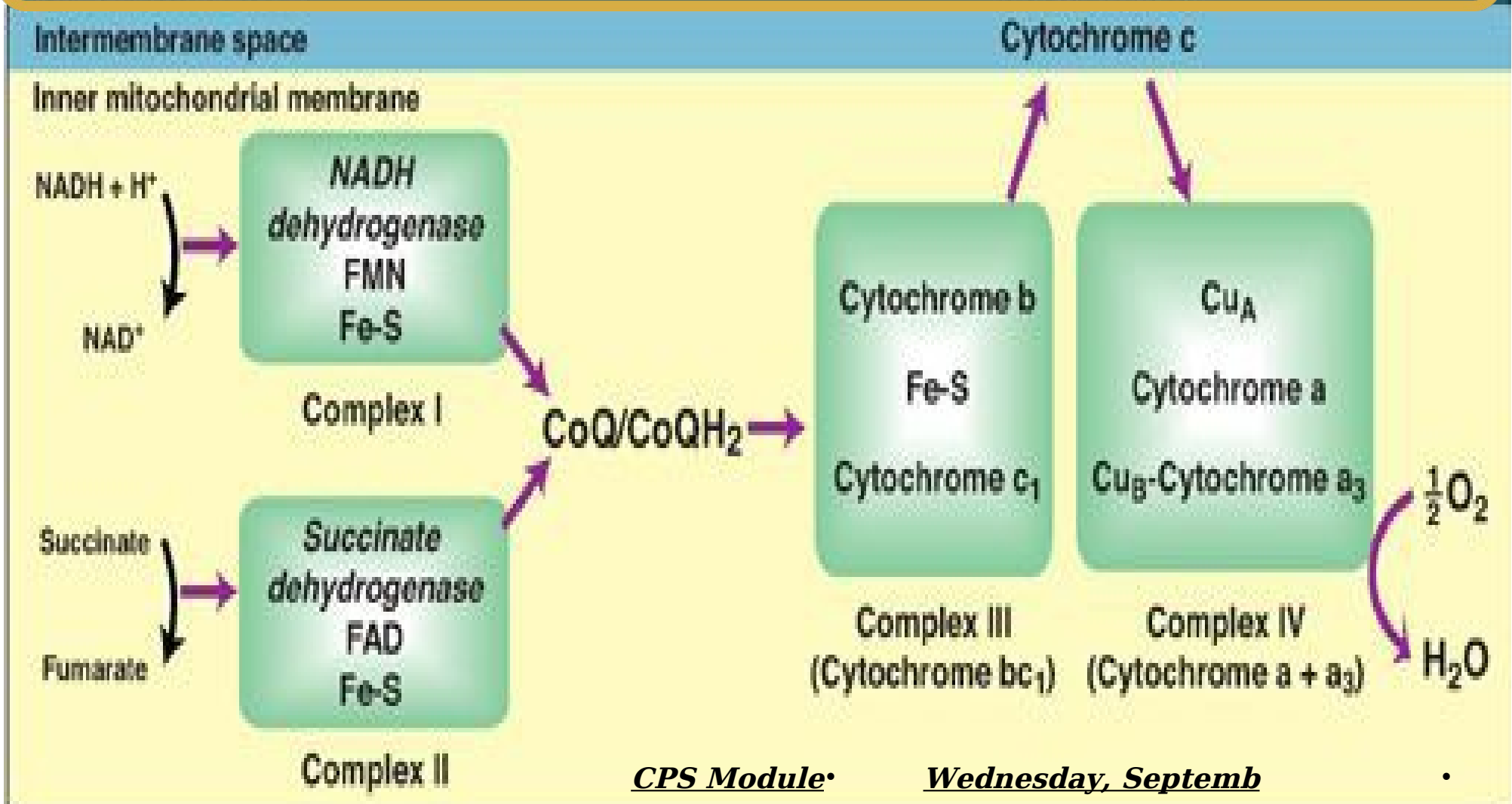
Contrary to cytochromes, iron is not present in heme but in association with inorganic sulfur atoms or with sulfur atoms of cysteine residues in the protein. Iron sulfur proteins participate in one electron transfer.

ETC components are arranged in the inner mitochondrial membrane forming **5 complexes**



- **Complex I** = NADH **Dehydrogenase**
- **Complex II** = Succinate **Dehydrogenase**
- **Complex III** = Cytochrome **C Reductase** (b-c₁)
- **Complex IV** = Cytochrome **C Oxidase** (a-a₃)
- **Complex V** = **ATP synthase Complex**

Respiratory chain consist of enzymatic complexes



Arrangements



The major components of the **ETC** are arranged **sequentially** in an order so that the **electrons flow** through the chain in a **stepwise manner** from the **e⁻ donors** molecules to the **e⁻ acceptor (with high e⁻ affinity)** i.e. oxygen.

This movement of electrons releases energy used in ATP synthesis.

Complex I



“NADH dehydrogenase”

It collects the ***NADH***

& associated with **CoQ**.

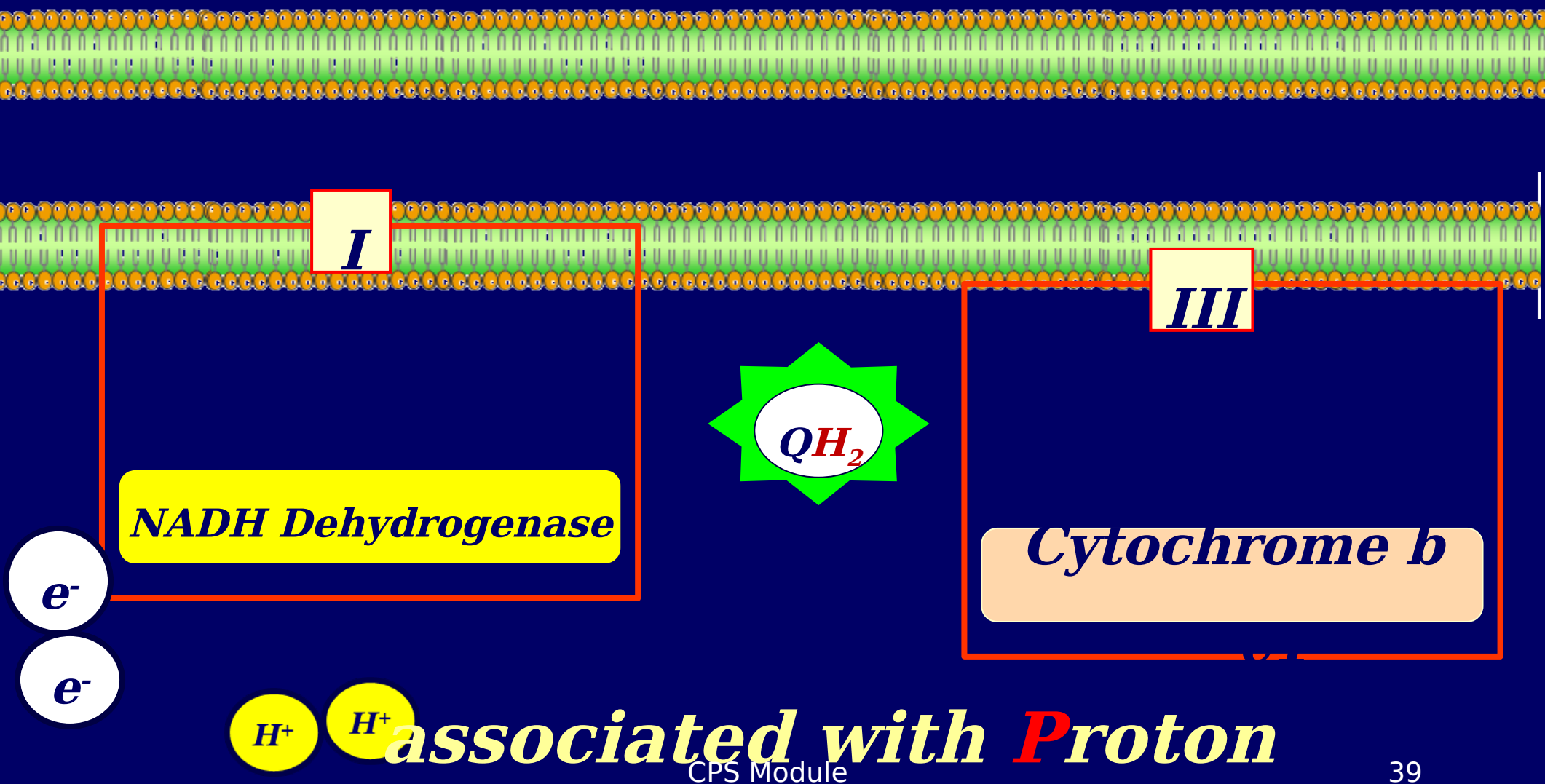
oxidation of one NADH and transfer of
two electrons to ubiquinone



Complex I

- During oxidation of one NADH and transfer of two electrons to ubiquinone by complex I, two protons are pumped across the mitochondrial membrane from the matrix side (N for negative face) to the cytosolic side (P for positive face). The energy released during oxidative reactions occurring in complex I is conserved by concomitant pumping of protons across membrane.

Complex I & Co Q



Complex II



“Succinate Dehydrogenase”
It is associated with CoQ

It is the **entry point of FADH₂**

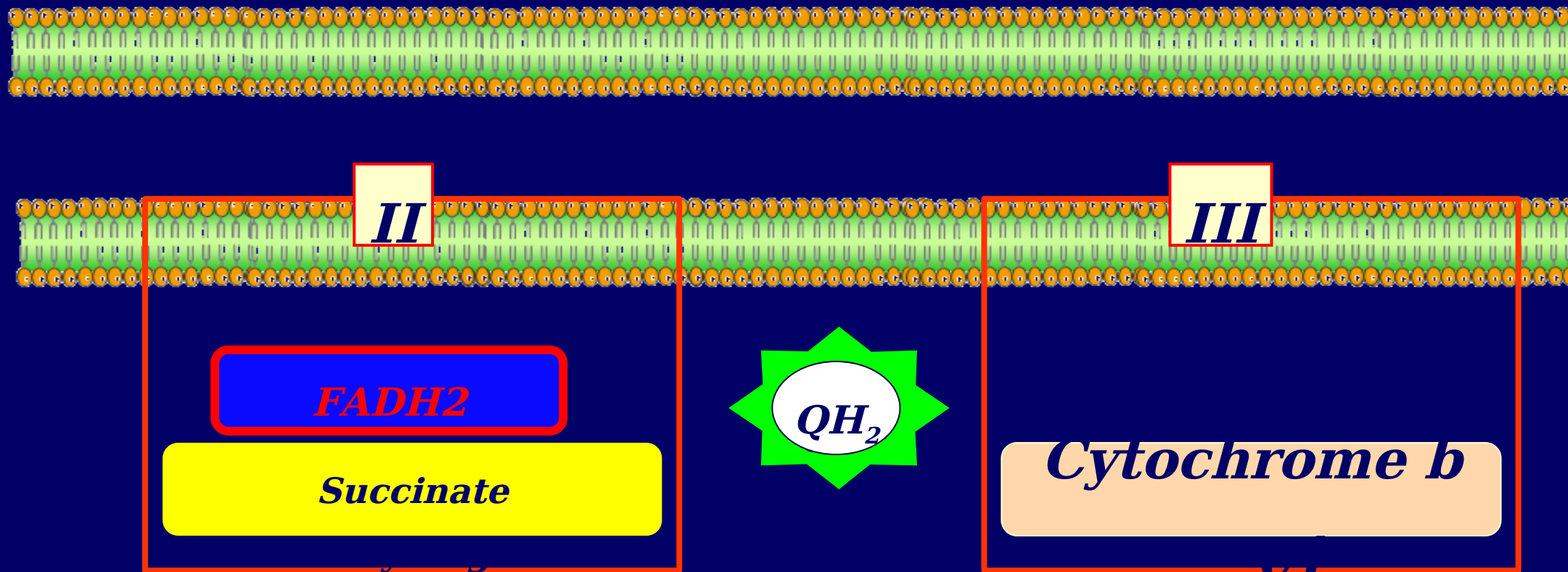
the transfer of electrons

from **FADH₂** to CoQ

It is Not associated with Proton Pump !!

Because It does Not ***traverse the whole length of the inner mitochondrial membrane.***

Complex II & Co Q



It is ~~Not~~ associated with Proton

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All of the following statements about the complex that carries out the synthesis of ATP during oxidative phosphorylation are correct except:

- (A) It is located on the inner mitochondrial membrane.
- (B) It is inhibited by Oligomycin
- (C) It contains F^o and F_1 subunits
- (D) It can bind molecular O_2
- (E) It is called complex V



Which of the Following is oxidized by the respiratory chain?

- a. NADPH
- b. Acetyl CoA.
- c. Oxygen.
- d. NAD+.
- e. NADH

SUGGESTED TEXTBOOKS



- ***"Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R. Ferrier.***
- ***"Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W. Rodwell.***

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